Applicants request a three-month extension of time to file this reply and enclose a check for the requisite fee in payment of the extension fees pursuant to 37 C.F.R. § 1.17(a)(3).

Please amend the application as follows:

IN THE SPECIFICATION:

On page 16, line 17, after "ECACC" and before "as Accession numbers" please insert --European Collection of Cell Cultures, CAMR (Center for Applied Microbiology and Research), Salisbury, Wiltshire, SP4 OJG, England,--

IN THE CLAIMS:

Please cancel claims 2, 5, 10-12 and 14.

Please amend claims 1, 3-4, 6-8, 13, and 15-24 as follows:

1. (Amended) A cell line [derived] obtained from a transgenic [mammal] rat comprising:

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene[; and] operably linked to

(ii) a cell type specific promoter.

3. (Amended) A ~~cell line~~ as claimed in claim 1 which is a neuronal cell line[, mammary cell line, liver cell line or kidney cell line].

SUB D2 B3

4. (Amended) A cell line as claimed in claim 3 in which the [cell line is a neuronal cell line and the ] cell type specific promoter is a human NF-L gene promoter.

SUB D3 B4

6. (Amended) A cell line as claimed in any of [the preceding claims] claims 1, 3, or 4 in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a SV40tsA58 gene.

7. (Amended) A cell line as claimed in any of claims 1 [to 5] , 3, or 4 in which the conditional oncogene, transforming gene, immortalising gene or the cell cycle affecting gene is a C Erb $\beta$2 gene or a TGF $\alpha$ gene.

8. (Amended) A cell line as claimed in claim 1 in which the conditional oncogene, transforming gene or the cell cycle affecting gene or immortalizing gene is a SV40tsA58 gene and the cell type specific promoter is a human NF-L gene promoter.

13. (Amended) A method [for] of producing a transgenic [mammal,] rat, comprising:

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(i) causing a female [mammal] rat to super-ovulate by supplying her with a regular supply of Follicle Stimulating Hormone (FSH) prior to mating;

(ii) mating or artificially inseminating the female [mammal] rat;

SUB E3

(iii) obtaining the resulting embryo from the female [mammal] rat; and

(iv) incorporating

SUB B5 E3 CONT.

(i) a conditional oncogene, transforming gene or immortalising gene or a cell cycle affecting gene[; and] operably linked to

(ii) a cell specific promoter into the genome of the [mammalian] rat embryo.

15. (Amended) A method a[n]s claimed in claim [14] 13 wherein the FSH is supplied continuously.

16. (Amended) A method as claimed in claims [14] 13 or 15 wherein the supply of FSH is from 2mg to 8mg and the FSH is supplied over a 1 to 4 day period.

SUB B6 E4

17. (Amended) A transgenic [mammal] rat whose germ cells and somatic cells contain

(i) a conditional oncogene, transforming gene or immortalising gene or a cell cycle affecting gene[; and] operably linked to

(ii) a cell type specific promoter as a result of chromosomal incorporation into the [mammalian] rat genome or into the genome of an ancestor of said [mammal] rat.

18. (Amended) A transgenic [mammal] rat as claimed in claim 17, wherein the [mammal is a rat and the] conditional oncogene, transforming gene, immortalising gene, or the cell cycle affecting gene is a C Erb $\beta$2 gene or a TGF $\alpha$ gene or a SV40tsA58 gene.

SUB D4

19. (Amended) A method of testing a material suspected of being a carcinogen, said method comprising [exposing a mammal produced according to a method of the invention] subjecting a rat according to claim 17 or 18 or a rat produced according to the method of any of claims 13 or 15 or an ancestor thereof or cells or tissue from a cell line of [the invention] any of claims 1, 3, 4, 6, 7, 8, or 9, to said material and detecting neoplasms as an indication of carcinogenicity.

R6

20. (Amended) A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising [treating] administering said material to a [mammal produced according to a method of the invention] rat according to claim 17 or 18 or a rat produced according to a method of claims 13 or 15 or an ancestor thereof or cells or tissues from a cell line of [the invention] any of claims 1, 3, 4, 6, 7, 8, or 9, [with said material] and detecting a reduced incidence of development or neoplasms, compared to an untreated [mammal] rat, as an indication of said protection.

21. (Amended) A method of [providing] obtaining a cell line comprising culturing a somatic cell obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or an ancestor thereof [according to the invention].

22. (Amended) A cell derived for a cell line obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or ancestor thereof [according to the invention].

23. (Amended) A method of [providing] obtaining a transgenic tissue comprising culturing a somatic cell obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or ancestor thereof[ according to the invention].

B6

24. (Amended) A tissue derived from a somatic cell obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or ancestor thereof[ according to the invention].

Please and add new claims 25-29 as follows:

SUB E5

B7

--25. A method of generating a cell line from a transgenic rat comprising a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to a cell specific promoter, the method comprising:

(i) maintaining the rat at restrictive conditions such that the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is expressed in vivo, only in a tissue of interest and in an inactive form such that the cells thereof grow normally;

(ii) culturing said cells from the tissue of interest in vitro under permissive conditions such that the immortalizing function is activated; and

(iii) subjecting the cells to non-permissive conditions so as to result in a cessation of growth and in differentiation.

26. A method as claimed in claim 25 wherein the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a temperature sensitive gene.

27. A method as claimed in claim 25 or 26 wherein the permissive condition is a temperature of 33°C and the restrictive condition is a temperature of 39°C.

28. A method of testing a material suspected of being a carcinogen, said method comprising administering said material to a rat produced according to the method of claim 16 or an ancestor thereof and detecting neoplasms as an indication of carcinogenicity.

29. A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising administering said material to a rat produced according to the method of claim 16 or an ancestor thereof and detecting a reduced incidence of development of neoplasms, compared to an untreated rat, as an indication of said protection.--

## REMARKS

Before amendment, claims 1-24 were pending. After amendment, claims 1, 3-4, 6-9, 13 and 15-29 are pending.

These amendments are supported throughout the present specification. No new matter is introduced by these amendments.